

(e) contacting the binding oligonucleotides with the first type of nanoparticles bound to the substrate, the contacting taking place under conditions effective to allow hybridization of the binding oligonucleotides with the oligonucleotides on the first type of nanoparticles;

(f) providing a second type of nanoparticles according to any one of Claims 243-250 having recognition oligonucleotides attached thereto, at least one of the types of recognition oligonucleotides on the second type of nanoparticles comprising a sequence complementary to the second portion of the sequence of the binding oligonucleotides;

(g) contacting the binding oligonucleotides bound to the substrate with the second type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the second type of nanoparticles with the binding oligonucleotides; and

(h) observing the detectable change.

365. The method of Claim 364 further comprising:

(i) contacting the second type of nanoparticles bound to the substrate with the binding oligonucleotides, the contacting taking place under conditions effective to allow hybridization of the binding oligonucleotides with the oligonucleotides on the second type of nanoparticles;

(j) contacting the binding oligonucleotides bound to the substrate with the first type of nanoparticles, the contacting taking place under conditions effective to allow hybridization of the oligonucleotides on the first type of nanoparticles with the binding oligonucleotides; and

(k) observing the detectable change.

366. The method of Claim 365 wherein steps (e) and (g) or steps (e), (g), (i) and (j) are repeated one or more times, and the detectable change is observed.

367. The method of Claim 360 wherein the substrate is a transparent substrate or an opaque white substrate.

368. The method of Claim 367 wherein the detectable change is the formation of dark areas on the substrate.

369. The method of Claim 360 wherein the nanoparticles are metal nanoparticles or semiconductor nanoparticles.

370. The method of Claim 369 wherein the nanoparticles are made of gold or silver.

371. The method of Claim 360 wherein the substrate has a plurality of types of oligonucleotides attached to it in an array to allow for the detection of multiple portions of a single nucleic acid, the detection of multiple different nucleic acids, or both.

372. The method of Claim 360 wherein the substrate is contacted with silver stain to produce the detectable change.

373. The method of Claim 371 wherein the substrate is contacted with silver stain to produce the detectable change.

375. The method of Claim 360 wherein the detectable change is observed with an optical scanner

376. The method of Claim 375 wherein the device is a flatbed scanner.

377. The method of Claim 375 wherein the scanner is linked to a computer loaded with software capable of calculating greyscale measurements, and the greyscale measurements are calculated, to provide a quantitative measure of the amount of nucleic acid detected.

378. The method of Claim 360 wherein the oligonucleotides attached to the substrate are located between two electrodes, the nanoparticles are made of a material which is a conductor of electricity, and the detectable change is a change in conductivity.

379. The method of Claim 378 wherein the electrodes are made of gold, and the nanoparticles are made of gold.

380. The method of Claim 378 wherein the substrate is contacted with silver stain to produce the change in conductivity.

381. The method of Claim 371 wherein each of the plurality of oligonucleotides attached to the substrate in the array is located between two electrodes, the nanoparticles are made of a material which is a conductor of electricity, and the detectable change is a change in conductivity.

382. The method of Claim 381 wherein the electrodes are made of gold, and the nanoparticles are made of gold.

383. The method of Claim 381 wherein the substrate is contacted with silver stain to produce the change in conductivity.

384. A method of detecting a nucleic acid having at least two portions comprising: